Network Systems
Science & Advanced
Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

March 30th, 2022

(data current to March 26th – March 29th)
Biocomplexity Institute Technical report: TR 2022-021



BIOCOMPLEXITY INSTITUTE

biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



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Overview

• Goal: Understand impact of COVID-19 mitigations in Virginia

Approach:

- Calibrate explanatory mechanistic model to observed cases
- Project based on scenarios for next 4 months
- Consider a range of possible mitigation effects in "what-if" scenarios

Outcomes:

- Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
- Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rates and hospitalizations are starting to plateau
- VA 7-day mean daily case rate slowly decreased to 8/100K from 10/100K
 - US has plateaued to 9/100K (from 9/100K)
- BA.2 subvariant of Omicron approaches 50% prevalence and continues to grow
- Projections anticipate a plateau at moderate to low levels, though growth from BA.2 or other factors is possible:
 - Future levels and resilience to new variants and reduced infection control measures depend on the strength of immunity gained through infection with Omicron and its durability against waning
- Model updates:
 - Adjusted ascertainment levels during Omicron to better capture degraded case detection and reduced symptomatic fraction of Omicron
 - Further calibration of model parameters to match recent data on population immunity post-Omicron wave continue and will provide better longterm estimates of future disease dynamics

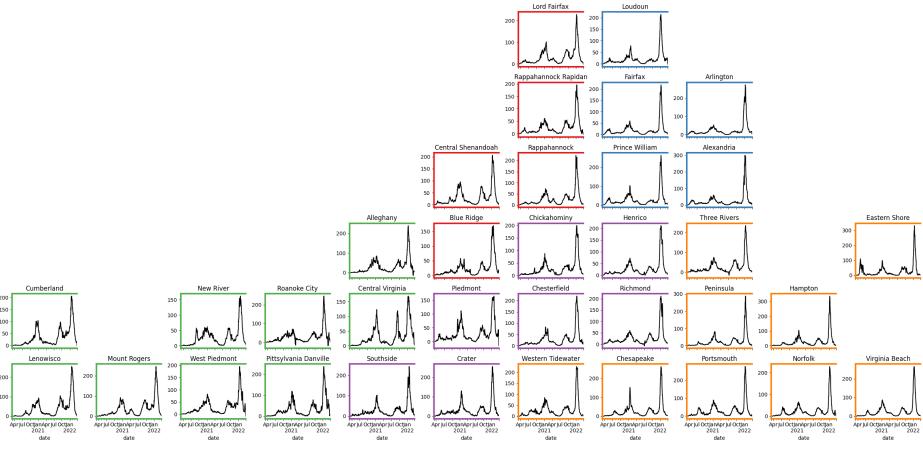
The situation continues to change. Models continue to be updated regularly.

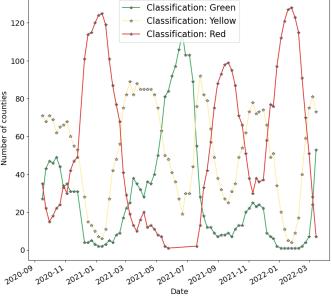
31-Mar-22

Situation Assessment



Case Rates (per 100k) and Test Positivity





County level RT-PCR test positivity

Green: <5.0% (or <20 tests in past 14 days)
Yellow: 5.0%-10.0% (or <500 tests and <2000
tests/100k and >10% positivity over 14 days)
Red: >10.0% (and not "Green" or "Yellow")

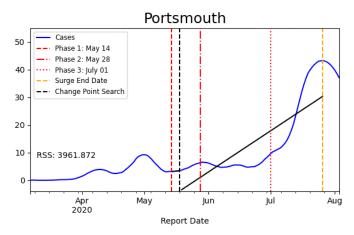


District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit



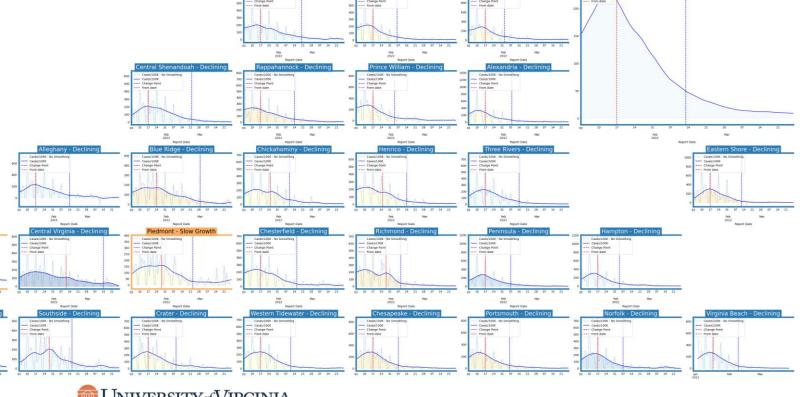
Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	32 (31)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	0 (1)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	3 (3)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	0 (0)



District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	32 (31)
Plateau	0 (1)
Slow Growth	3 (3)
In Surge	0 (0)

Curve shows smoothed case rate (per 100K) Trajectories of states in label & chart box Case Rate curve colored by Reproductive number



■ 1.5 <= R < 2

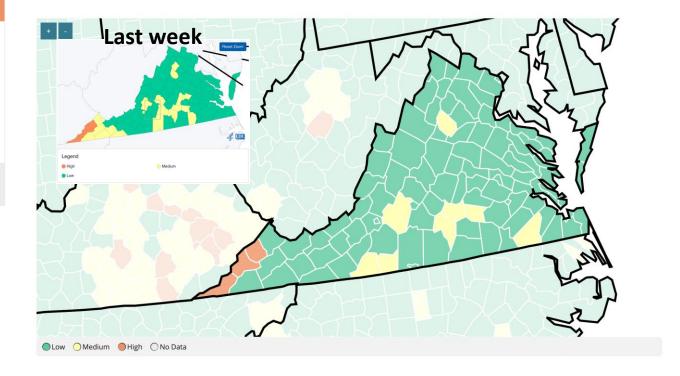
 $0.2 \le R \le 0.5$

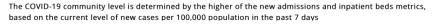
CDC's new COVID-19 Community Levels

What Prevention Steps Should You Take Based on Your COVID-19 Community Level?

Low	Medium	High			
 Stay <u>up to date</u> with COVID-19 vaccines <u>Get tested</u> if you have symptoms 	 If you are at high risk for severe illness, talk to your healthcare provider about whether you need to wear a mask and take other precautions Stay up to date with COVID-19 vaccines Get tested if you have symptoms 	 Wear a mask indoors in public Stay up to date with COVID-19 vaccines Get tested if you have symptoms Additional precautions may be needed for people at high risk for severe illness 			
People may choose to mask at any time. People with symptoms, a positive test, or exposure to someone with COVID-19					

COVID-19 Community Levels – Use the Highest Level that Applies to Your Community							
New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High			
Fewer than 200	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0			
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	<10.0%	10.0-14.9%	≥15.0%			
200 or more	New COVID-19 admissions per 100,000 population (7-day total)	NA	<10.0	≥10.0			
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	NA	<10.0%	≥10.0%			



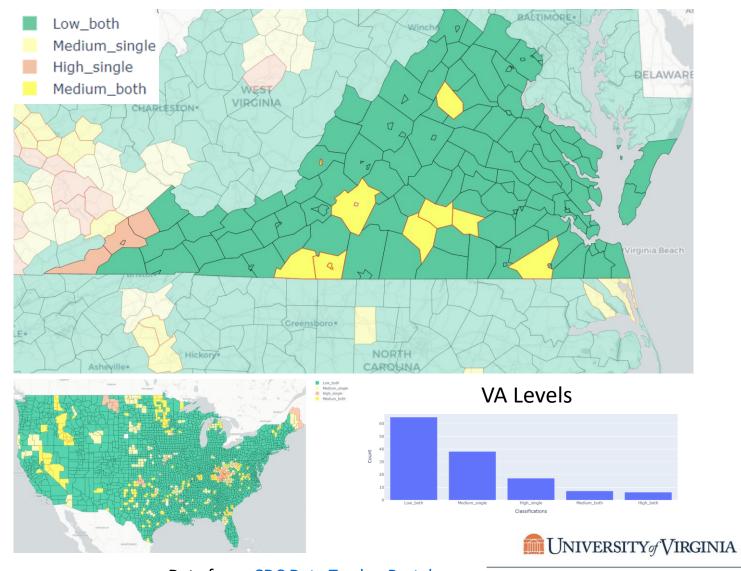




CDC Data Tracker Portal

should wear a mask.

CDC's new COVID-19 Community Levels



Red outline indicates county had 200 or more cases per 100k in last week

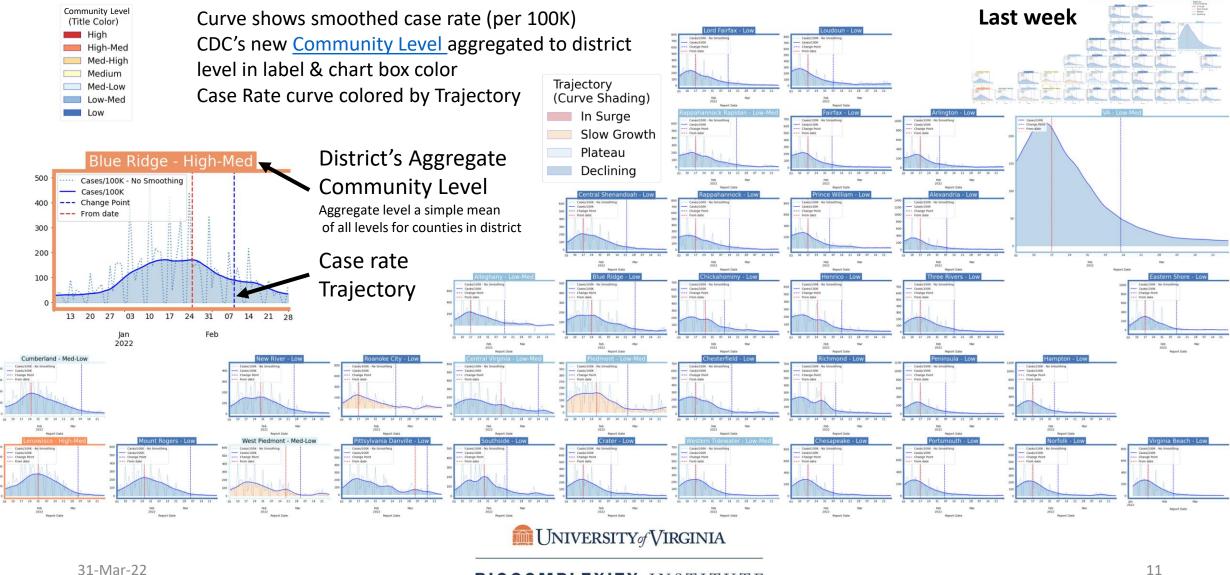
Pale color indicates either beds or occupancy set the level for this county

Dark color indicates both beds and occupancy set the level for this county

COVID-19 Community Levels – Use the Highest Level that Applies to Your Community						
New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High		
Fewer than 200	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0		
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	<10.0%	10.0-14.9%	≥15.0%		
	New COVID-19 admissions per 100,000 population (7-day total)	NA	<10.0	≥10.0		
200 or more	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	NA	<10.0%	≥10.0%		

The COVID-19 community level is determined by the higher of the new admissions and inpatient beds metrics, based on the current level of new cases per 100,000 population in the past 7 days

District Trajectories with Community Levels

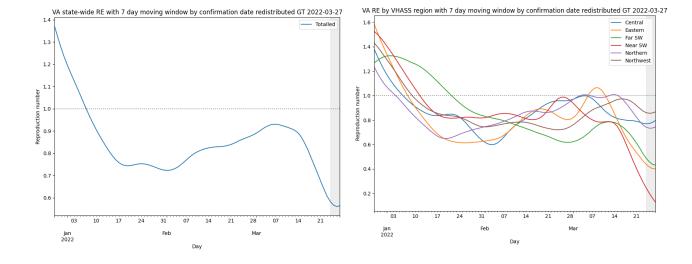


Estimating Daily Reproductive Number –

Redistributed gap

March 28th Estimates

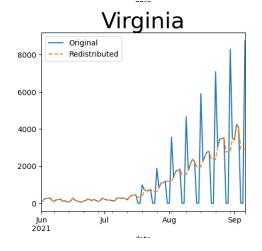
Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.787	0.194
Central	0.982	0.585
Eastern	0.823	0.387
Far SW	0.527	0.071
Near SW	0.132	-0.537
Northern	0.912	0.095
Northwest	0.958	0.302



Skipping Weekend Reports & holidays biases estimates Redistributed "big" report day to fill in gaps, and then estimate R from "smoothed" time series

Methodology

- Wallinga-Teunis method (EpiEstim¹) for cases by confirmation date
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

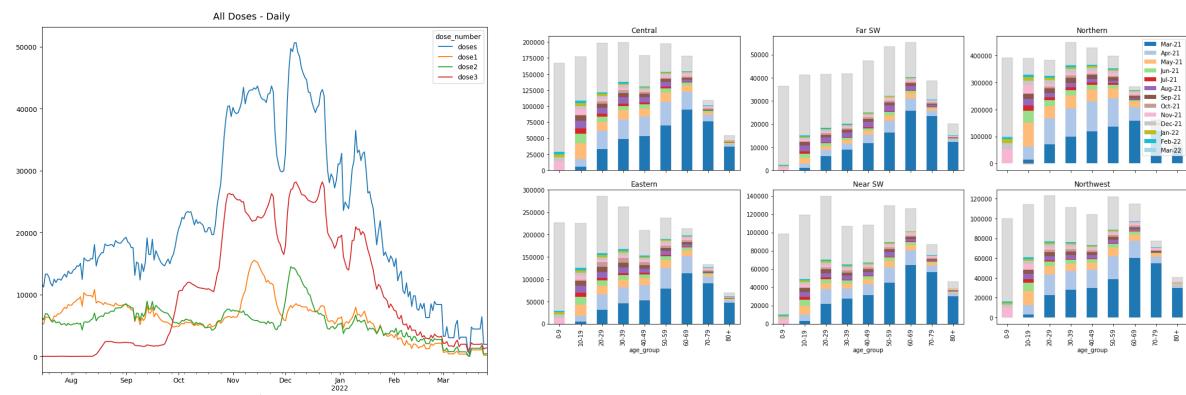


^{1.} Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Vaccination Administration in Virginia

Vaccine Doses administered:

- Doses administered rates continue to slow into a low-level plateau
- Considerable reduction in vaccination rate experienced since mid-January
- Third dose administration remains highest

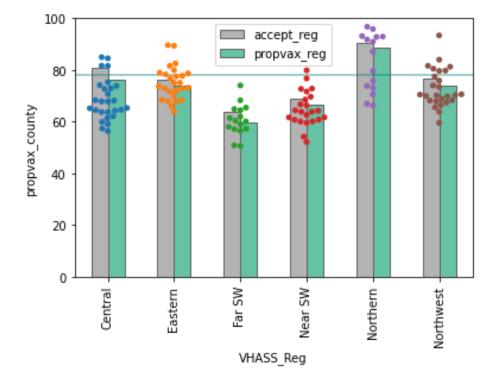


Vaccination Acceptance by Region

Corrections to surveys:

- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
 - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
 - Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

Region	COVIDcast accepting corrected	VDH proportion pop vaccinated
Central	82%	76%
Eastern	77%	74%
Far SW	64%	60%
Near SW	69%	66%
Northern	91%	88%
Northwest	77%	74%
Virginia	81%	78%



Grey Bar: Survey measured and corrected acceptance

Green Bar: Proportion of eligible population

administered a vaccine

Dots: Proportion administered at least one dose for

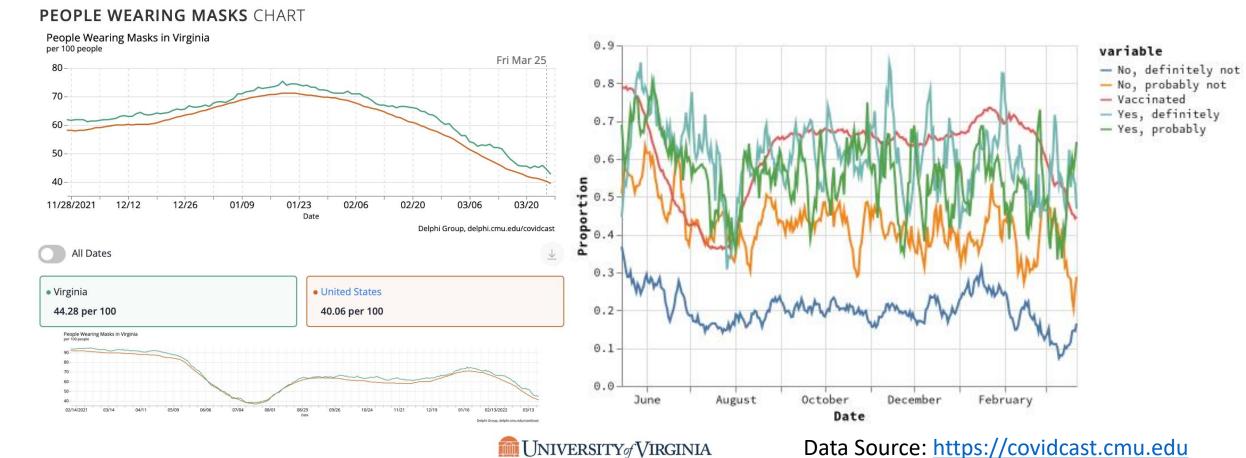
each county



Mask Usage Slows and Continues Decline

Self-reported mask usage drops to nearly lowest level of pandemic in July 2021

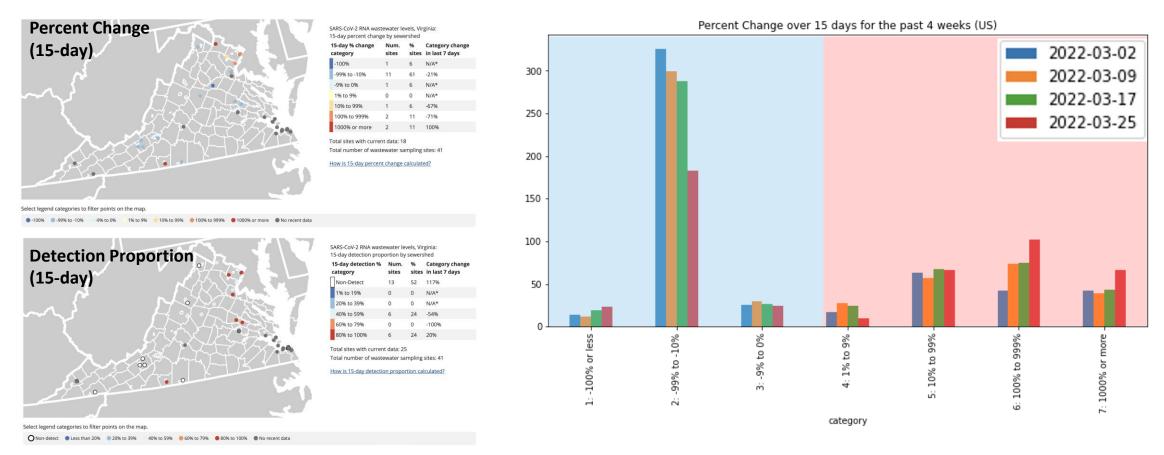
- US and VA experienced similar decreases, though VA remains slightly higher
- Mask wearing remains lower amongst unvaccinated especially among least willing to be vaccinated



Wastewater Monitoring

Wastewater provides a coarse early warning of COVID-19 levels in communities

- Most sites in Northern and Eastern continue to detect COVID-19 in wastewater, Western part of state has no detection
- General US trend in last couple weeks to have more increases in the level of virus detected



Data Source: CDC Data Tracker



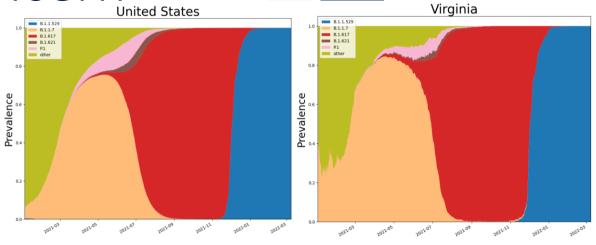
SARS-CoV2 Variants of Concern

Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
 - Increase transmissibility
 - Increase severity (more hospitalizations and/or deaths)
 - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
 - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L	+R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

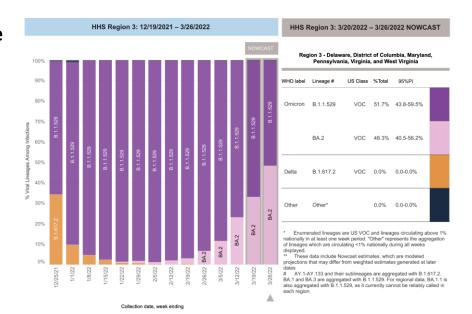




Omicron Prevalence CDC now tracking subvariant BA.2

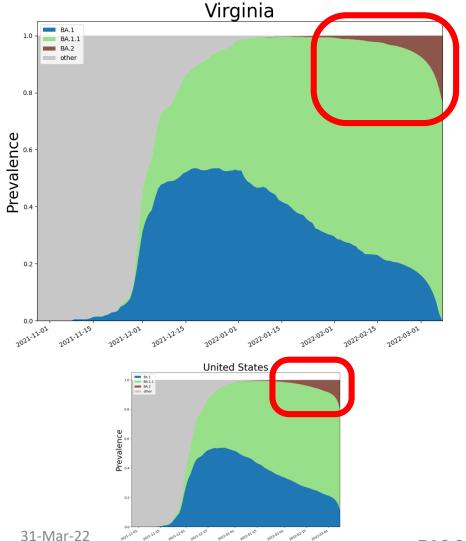
CDC nowcast for week ending March 26th shows 48% BA.2 in Region 3, up from 33% previous week

Nationally BA.2 is now the predominant subvariant (55%)

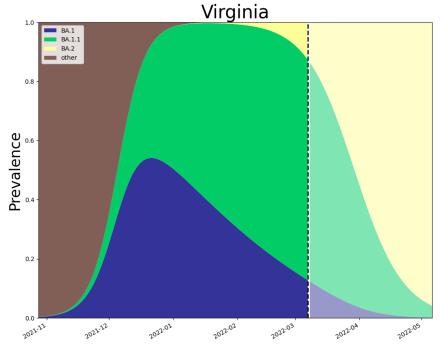


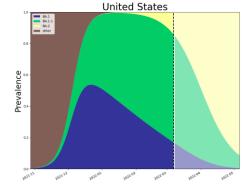
SARS-CoV2 Omicron and Sub-Variants

As detected in whole Genomes in public repositories



VoC Polynomial Fit Projections





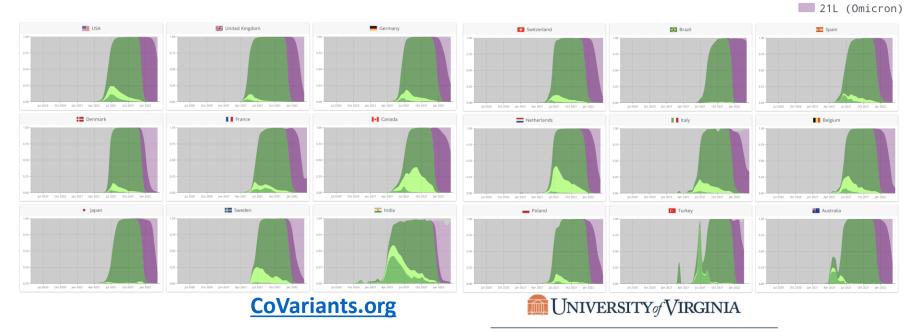
Note: Data lags force projections to start in past. Everything from dotted line forward is a projection.

GISAID

SARS-CoV2 BA.2 subvariant Tracking

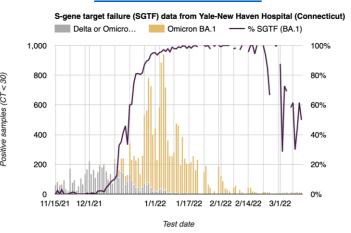
BA.2 subvariant growing rapidly in some European countries

- Both Delta and the Omicron BA.2 subvariant don't have the SGTF signal with PCR tests, so the reduction in SGTF from BA.1 can be an imperfect signal for increased BA.2
- BA.2 is now majority subvariant in most northern European countries and India and some neighbors



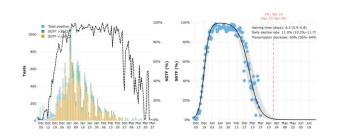
SGTF proxy in US

Yale- New Haven



San Diego

21A (Delta)
21I (Delta)
21J (Delta)
21J (Delta)
21K (Omicron)



SGTF in CT and CA indicate majority Are BA.2 subvariants now

Pandemic Pubs

- 1
- **1.** Financial Times graphics nicely illustrate the impact of BA.2 on several European countries.
- 2. New analysis in UK HSA report illustrates that VE against hospitalization remains high even for 65+ (85%) when corrected for hospitalization likely due to COVID.
- **3.** Researchers in Sweden find nasal swabs from BA.2 give two-fold higher levels of RNA.
- **4.** New research in MMWR shows significantly improved protection for those who follow a primary J&J vaccine with an mRNA booster.

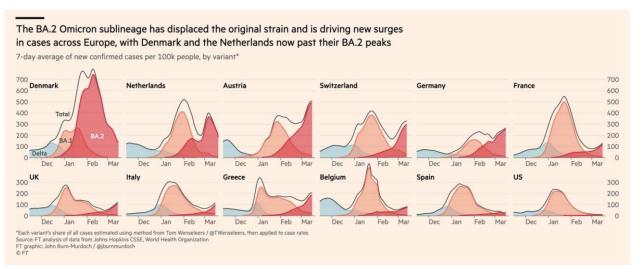


TABLE 2. Vaccine effectiveness* of 1 primary Janssen vaccine dose, homologous and heterologous boosters following primary Janssen vaccination, and 3 mRNA COVID-19 vaccine doses' against laboratory-confirmed COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults aged 18 vears* — VISION Network. 10 states. December 2021—March 2022*

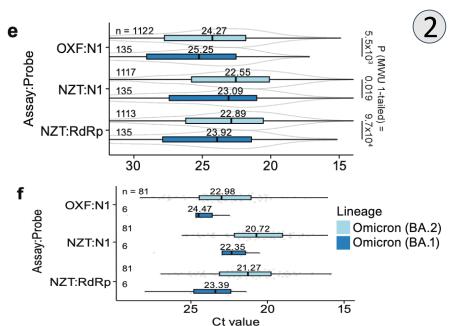
Medical event, vaccination status (days since most recent dose)	Total	Positive SARS-CoV-2 result, no. (%)	VE %* (95% CI)
ED/UC events (N = 80,287)			
Unvaccinated (Ref)	52,025	23,560 (45.3)	Ref
1 Janssen dose ≥14 days earlier (median = 262 days [range = 196–293])	4,514	1,652 (36.6)	24 (18-29
2 Janssen doses (7–120 days)	467	135 (28.9)	54 (43-63
1 Janssen/1 mRNA dose (7–120 days)	1,271	166 (13.1)	79 (74-8
3 mRNA doses (7–120 days)	22,010	2,614 (11.9)	83 (82-8
Hospitalizations (N = 25,244)			
Unvaccinated (Ref)	15,424	7,271 (47.1)	Ref
1 Janssen dose ≥14 days earlier (median = 264 days [range = 199-294])	1,451	518 (35.7)	31 (21-4
2 Janssen doses (7–120 days)	164	47 (28.7)	67 (52-7
1 Janssen/1 mRNA dose (7–120 days)	373	59 (15.8)	78 (70-8
3 mRNA doses (7–120 days)	7,832	775 (9.9)	90 (88-9

VE against COVID-19—associated emergency department/urgent care visits was 24% after 1 Jansen dose, 54% after 2 Jansen doses, and 79% after 1 Janssen/1 mRNA dose, compared to 83% after 3 mRNA doses. VE for the same strategies against COVID-19—associated hospitalization was 31%, 67%, 78%, and 90% respectively.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7113e2.htm?s_cid=mm7113e2_w#contrib



Financial Times Graphics based on JHU CSSE data



Analysis of 174,933 clinical nasopharyngeal swab samples using a custom variant-typing RT-PCR assay gives two-fold higher levels of viral RNA in cases with Omicron BA.2. Researchers developed a modified RT-PCR test to assess BA.1 status (panel E) and confirmed with sequencing (panel F)

https://www.medrxiv.org/content/10.1101/2022.03.26.22272984v1

Table 1. vaccine effectiveness against hospitalisation using different definintions of hospitalisations in a) 18 to 64 year olds and b) 65 year olds and over

		ECDS symptomatic with onset date	SUS at least 2 days with ARI code in primary field	SUS at least 2 days 8 either oxygen, ventilation or ICU with ARI code in primary field
		18 t	o 64	
	Interval	VE	VE	VE
Dose 1	0 to 27	48.5 (12.3 to 69.7)	36.2 (-33.9 to 69.6)	
	28+	48.7 (32.8 to 60.8)	44.1 (25.6 to 58)	75 (42.4 to 89.1)
Dose 2	0 to 13	39.6 (-31.5 to 72.2)	88.9 (58.4 to 97)	
	14 to 174	54.7 (45.3 to 62.4)	69 (58.1 to 77)	86.7 (63.6 to 95.1)
	175+	34.6 (21.7 to 45.4)	56.1 (46.4 to 64)	82.3 (67.7 to 90.3)
Booster	0 to 6	63.9 (52.2 to 72.8)	74.3 (55.9 to 85)	90.7 (56 to 98.1)
	7 to 13	80.1 (73.5 to 85.1)	90.9 (83.2 to 95.1)	0 (100 to 100)
	14 to 34	82.4 (78.6 to 85.6)	88.6 (84.9 to 91.5)	97.1 (92.2 to 98.9)
	35 to 69	72.7 (67.2 to 77.2)	85.8 (82.4 to 88.5)	94.3 (88.9 to 97.1)
	70 to 104	66.9 (59.1 to 73.3)	80.2 (74.9 to 84.4)	89.9 (78.3 to 95.3)
	105+	53.6 (36.9 to 65.9)	67.4 (53.1 to 77.4)	75.9 (15.8 to 93.1)
		6	5+	
	Interval	VE	VE	VE
Dose 1	0 to 27		43.9 (-41 to 77.7)	
	28+		53.4 (36.3 to 65.9)	78.3 (43.7 to 91.7)
Dose 2	0 to 13		0 (100 to 100)	
	14 to 174	77.8 (45 to 91)	82.3 (74.3 to 87.8)	90.9 (72.6 to 97)
	175+	66.7 (43.4 to 80.4)	57.7 (49.6 to 64.4)	73.4 (55.1 to 84.3)
Booster	0 to 6	85.8 (61.5 to 94.7)	77.9 (65.3 to 85.9)	89.2 (63.1 to 96.8)
	7 to 13	92.3 (76.3 to 97.5)	84.7 (76 to 90.2)	94.7 (71.6 to 99)
	14 to 34	92.4 (86 to 95.8)	91.3 (89.1 to 93.1)	95.8 (91.3 to 97.9)
	35 to 69	87 (79.2 to 91.8)	89.3 (87.3 to 90.9)	92.8 (88.4 to 95.6)
	70 to 104	84 (74.6 to 89.9)	88.1 (86.1 to 89.9)	92.5 (88.1 to 95.2)
	105+	76.9 (60.6 to 86.4)	85.3 (82.4 to 87.6)	86.8 (77.1 to 92.3)

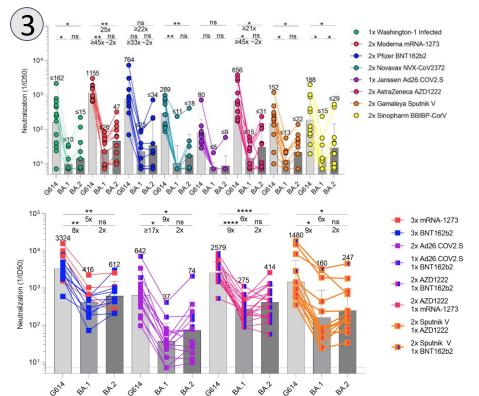
ECDS = Emergency Care Dataset (this analysis includes all admissions with a positive COVID-19 test via emergency care except for those coded as injuries); SUS = Secondary Users Service (this analysis includes all admissions to secondary care for >=2 days with a respiratory code in the first diagnostic field) (10).

Using medical records analyzed population level protection against hospitalization due to respiratory illness for more than 2 days

UK HAS report (24 March 2022)

Pandemic Pubs (last week)

- 1. CDC Study Vaccine effectiveness against severe outcomes higher after a 3rd dose than after the 2nd, though wanes with time
- 2. High immunogenicity of mRNA vaccines is achieved after three doses with antibody levels restored by a fourth dose. Fourth dose displayed reduced vaccine efficacy against infections in young health care workers
- 3. Though Omicron BA.1 and BA.2 evade human plasma neutralizing antibodies elicited by infection or primary vaccine series, mRNA booster doses rescue neutralization potency across many initial vaccine types.

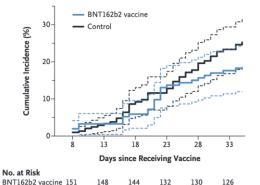


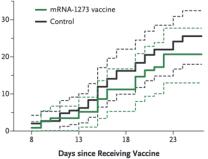
Characteristic	Total	SARS-CoV-2 positive test result no. (%)	VE fully adjusted % (95% CI)*	Waning trend p value††
Any mRNA vaccine, 3 doses	10,957	471 (4)	93 (92–94)	<0.001
<2 mos	7,332	221 (3)	95 (94–95)	10.001
2-3 mos	3,413	211 (6)	91 (89–92)	
≥4 mos	212	39 (18)	81 (72–87)	
Delta-predominant period				
Unvaccinated (Ref)	36,214	14,445 (40)	_	_
Any mRNA vaccine, 2 doses	38,707	3,315 (9)	85 (84-85)	<0.001
<2 mos	1,574	49 (3)	94 (92–96)	
2-3 mos	2,790	154 (6)	91 (89–92)	
4 mos	3,129	192 (6)	90 (89–92)	
≥5 mos	31,214	2,920 (9)	82 (82-83)	
Any mRNA vaccine, 3 doses	8,124	195 (2)	95 (95-96)	<0.001
<2 mos	6,071	118 (2)	96 (95–97)	
2–3 mos	2,030	74 (4)	93 (91-95)	
≥4 mos	23	3 (13)	76 (14-93)	
Omicron-predominant period				
Unvaccinated (Ref)	3,911	1,890 (48)	_	_
Any mRNA vaccine, 2 doses	3,619	979 (27)	55 (50-60)	0.01
<2 mos	88	22 (25)	71 (51–83)	
2–3 mos	294	69 (23)	65 (53-74)	
4 mos	150	42 (28)	58 (38-71)	
≥5 mos	3,087	846 (27)	54 (48-59)	
Any mRNA vaccine, 3 doses	2,833	276 (10)	88 (86-90)	<0.001
<2 mos	1,261	103 (8)	91 (88-93)	
2–3 mos	1,383	137 (10)	88 (85-90)	
≥4 mos	189	36 (19)	78 (67-85)	

"Vaccine effectiveness (VE) against COVID-19—associated emergency department/urgent care (ED/UC) visits and hospitalizations was higher after the third dose than after the second dose but waned with time since vaccination. During the Omicron-predominant period, VE against COVID-19associated ED/UC visits and hospitalizations was 87% and 91%, respectively, during the 2 months after a third dose and decreased to 66% and 78% by the fourth month after a third dose. Protection against hospitalizations exceeded that against ED/UC visits." https://www.cdc.gov/mmwr/volumes/71/wr/mm7107e2.htm?s cid=mm7107e2 w

This nonrandomized clinical study, assessed the immunogenicity and safety of a fourth dose of either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) administered 4 months after the third dose in a series of three BNT162b2 doses. Vaccine efficacy was estimated to be higher for the prevention of symptomatic disease (43% for BNT162b2 and 31% for mRNA-1273) https://www.neim.org/doi/pdf/10.1056/ NEJMc2202542?articleTools=true

C Efficacy against SARS-CoV-2 Infection





No. at Risk mRNA-1273 vaccine 115

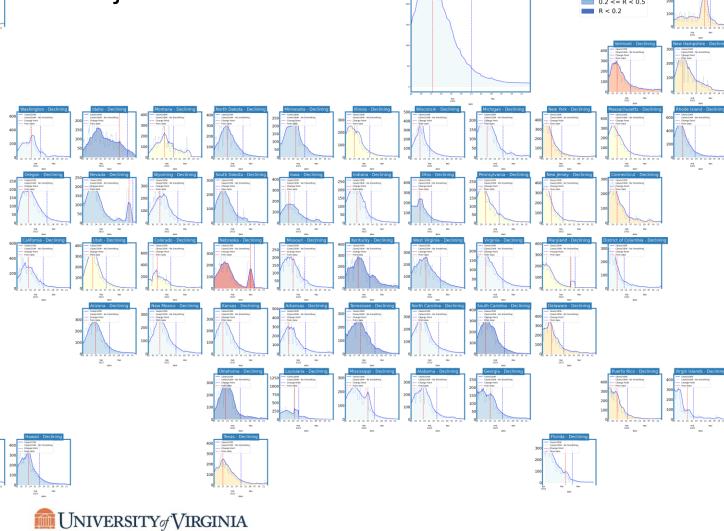
https://www.biorxiv.org/content/10.1101/2022.03.15.484542v1.full.pdf

United States Case Rates

All states have shifted to a declining trajectory



Trajectories of States

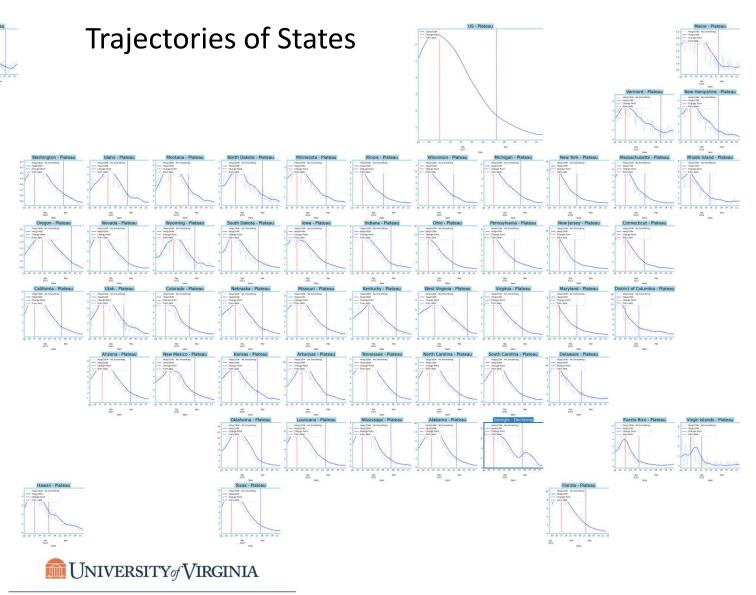


Status	# States
Declining	54 (54)
Plateau	0 (0)
Slow Growth	0 (0)
In Surge	0 (0)

United States Hospitalizations

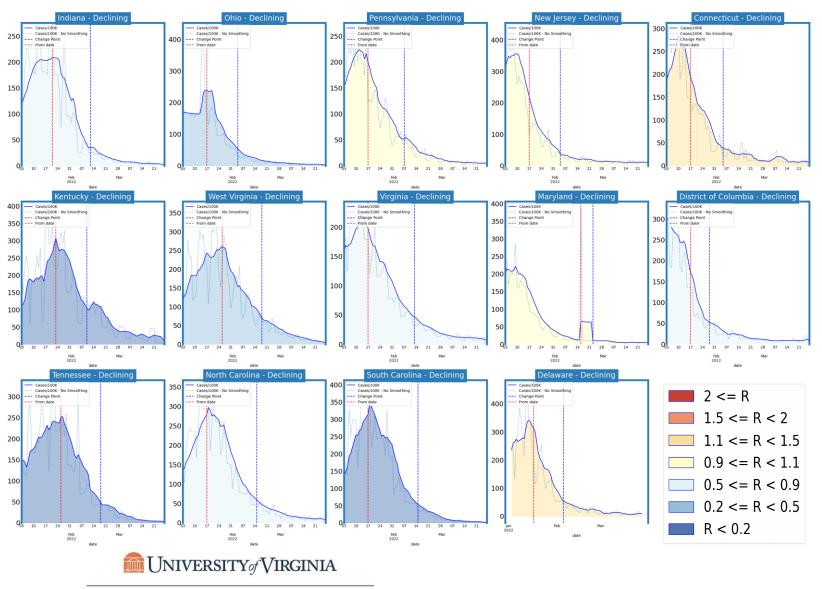
- Hospital admissions are lagging case rates, and have mainly entered plateaus
- Many states in growth trajectories show signs of slowing

Status	# States
Declining	1 (3)
Plateau	52 (50)
Slow Growth	0 (1)
In Surge	0 (0)



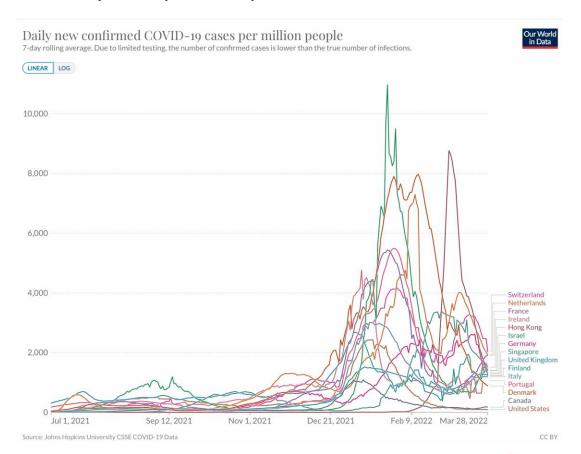
Virginia and Her Neighbors

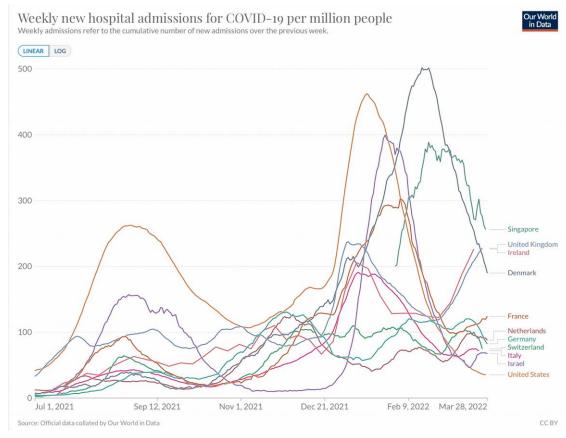
- All have dramatically dropped from peaks
- Rates have moderated
- All but Kentucky are below 10/100K



Other Countries

- Many, but not all, European countries are experiencing a rebound in cases
- Rebound in hospitalizations is a bit delayed but observed in some of these countries as well
- US per capita hospitalization rates lower than most European nations



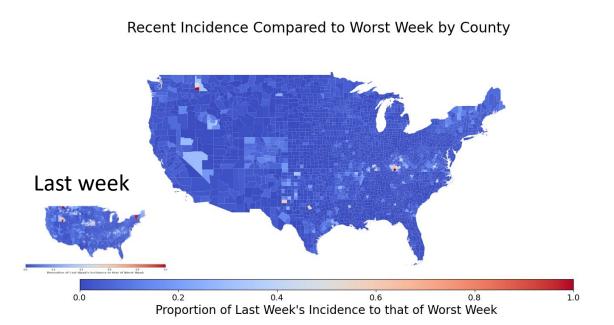


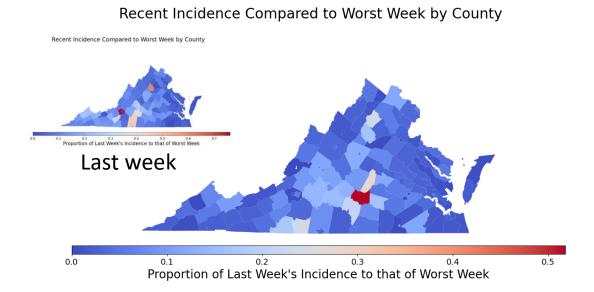


Our World in Data

County-level comparison to previous highest peak

- Most counties in VA have had the highest case rate of the pandemic in the last week
- Nationally the number of counties at their highest rate has expanded considerably

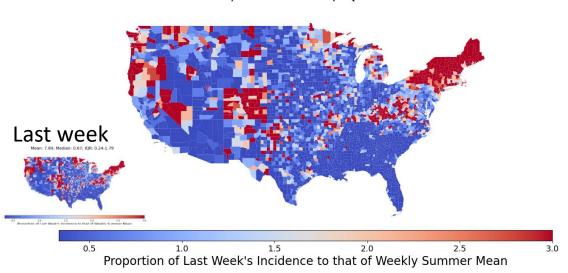


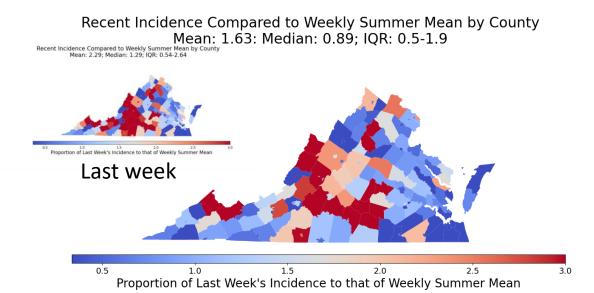


County-level comparison to last Summer

- Most counties in VA have had the highest case rate of the pandemic in the last week
- Nationally the number of counties at their highest rate has expanded considerably

Recent Incidence Compared to Weekly Summer Mean by County Mean: 8.95; Median: 0.51; IQR: 0.18-1.47



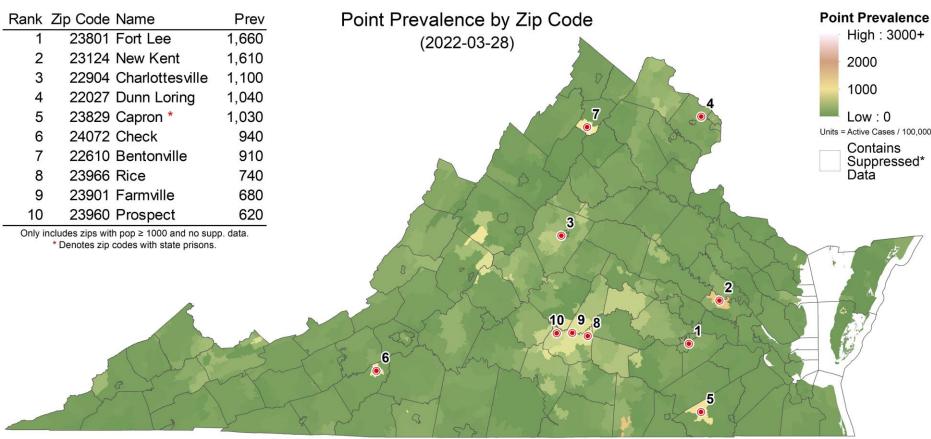




Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

- Clusters of high prevalence in Southwest
- Some counts are low and suppressed to protect anonymity, those are shown in white



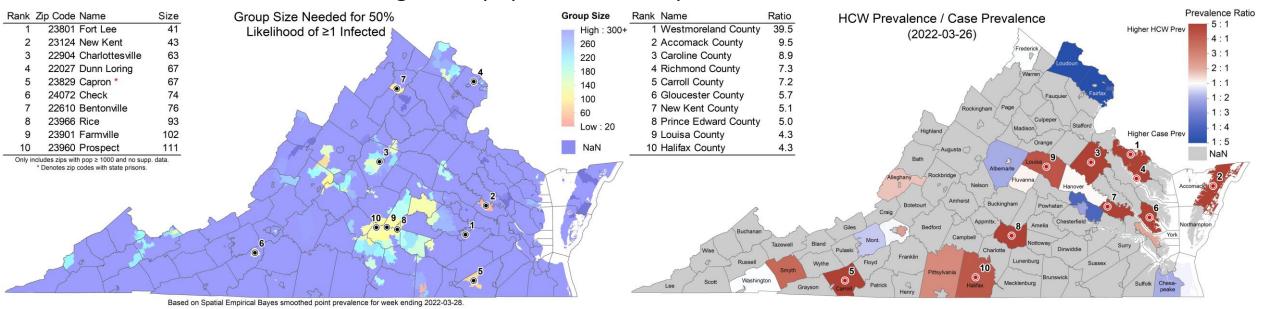
Based on Spatial Empirical Bayes smoothed point prevalence for week ending 2022-03-28.



Risk of Exposure by Group Size and HCW prevalence

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people (group size 25)

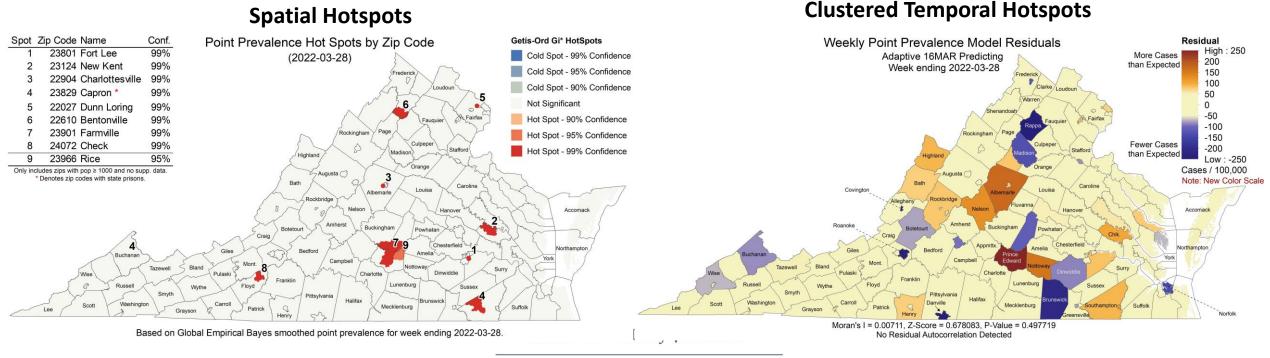
- **Group Size**: Assumes 2 undetected infections per confirmed case (ascertainment rate from recent seroprevalence survey), and shows minimum size of a group with a 50% chance an individual is infected by zip code (eg in a group of 41 in Fort Lee, there is a 50% chance someone will be infected)
- **HCW ratio**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator / general population's case prevalence



Current Hot-Spots

Case rates that are significantly different from neighboring areas or model projections

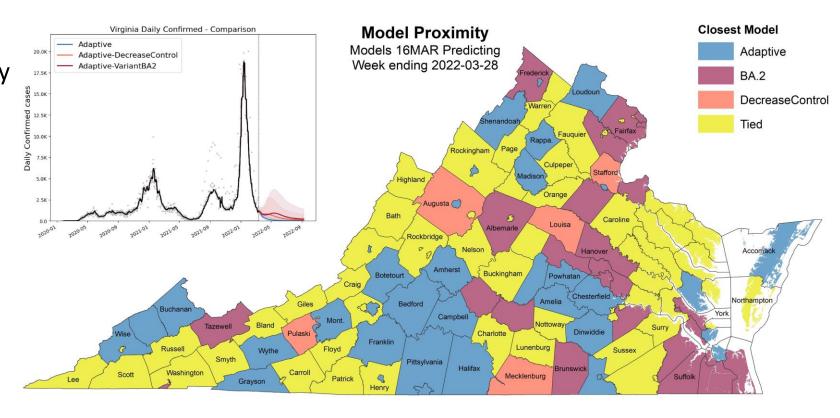
- **Spatial**: Getis-Ord Gi* based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections



Scenario Trajectory Tracking

Which scenario from last projection did each county track closest?

- Minimal difference between projections overall
- Mixed results reflective of similarity of scenarios, most counties tracking slower decline scenarios (BA2 and DecreaseControl)





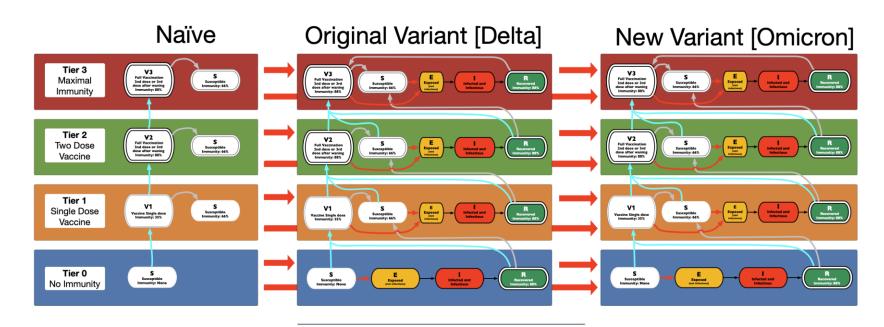
Model Update – Adaptive Fitting



Model Structure Extended for Multiple Strains

Omicron escapes immunity from vaccinated and those infected with Delta

- Multiple strain support allows representation of differential protection based on immunological history
- Severity of Outcomes varies by strain and level of immunity, thus allowing model to better capture hospitalizations and deaths from Omicron
- Adaptive fitting approach continues to use simulation to generate the full distribution of immune states across the population



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

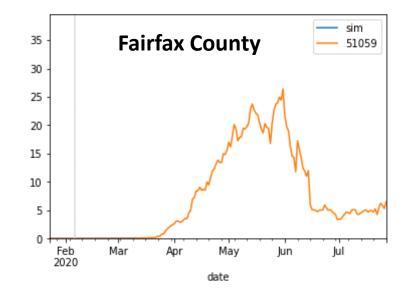
 Allows history to be precisely captured, and used to guide bounds on projections

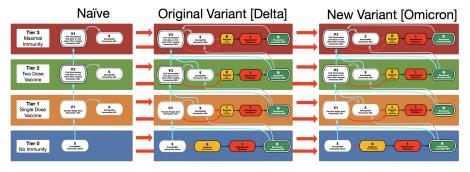
Model: An alternative use of the same meta-population model, PatchSim with multiple tiers of immunity

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Allows for waning of immunity and for partial immunity against different outcomes (eg lower protection for infection than death)

External Seeding: Steady low-level importation

 Widespread pandemic eliminates sensitivity to initial conditions, we use steady 1 case per 10M population per day external seeding







Using Ensemble Model to Guide Projections

Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

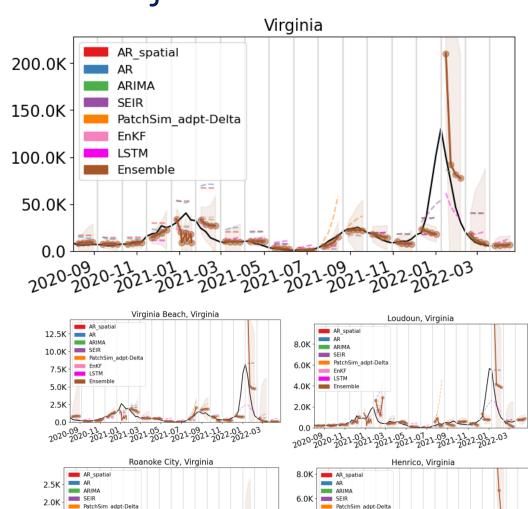
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

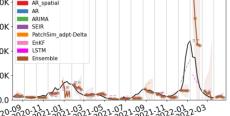
Weekly forecasts done at county level.

Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

Ensemble forecast provides additional 'surveillance' for making scenario-based projections.

Also submitted to CDC Forecast Hub.





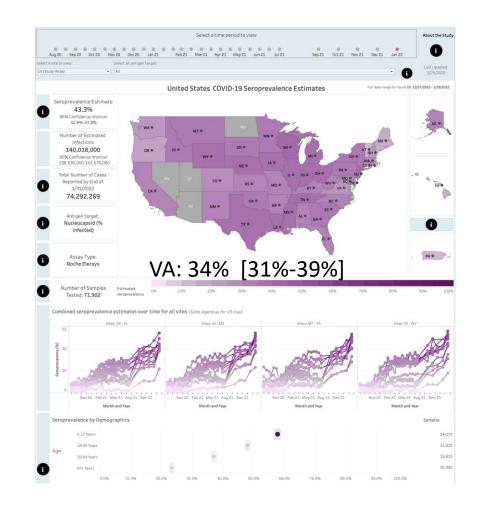
Seroprevalence updates to model design

Several seroprevalence studies provide better picture of how many actual infections have occurred

 CDC Nationwide Commercial Laboratory Seroprevalence Survey

Pre-Omicron these findings were consistent with an ascertainment ratio of ~2-3x

- Thus there were 2.5 total infections in the population for every confirmed case recently
- Case ascertainment for Omicron infections are half of that for pre-Omicron, thus for every case there are ~5 total infections
- During the peak of Omicron, the degradation of test seeking and capacity were modeled to have fallen by 3x with a rebound to pre-Omicron levels by mid-Feb.



https://covid.cdc.gov/covid-data-tracker/#national-lab



Calibration Approach

- Data:
 - · County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- Calibration: fit model to observed data and ensemble's forecast.
 - Tune transmissibility across ranges of:
 - Duration of incubation (5-9 days), infectiousness (3-7 days)
 - Undocumented case rate (1x to 7x) guided by seroprevalence studies
 - Detection delay: exposure to confirmation (4-12 days)
 - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- Project: future cases and outcomes generated using the collection of fit models run into the future
 - Mean trend from last 7 days of observed cases and first week of ensemble's forecast used
 - Outliers removed based on variances in the previous 3 weeks
 - 2 week interpolation to smooth transitions in rapidly changing trajectories
- Outcomes: Data driven by shift and ratio that has least error in last month of observations
 - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
 - Deaths: 11 days from confirmation, 1.45% of cases die



COVID-19 in Virginia:

Summarv

Dashboard Updated: 3/30/2022 Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths						
Total Cases* 1,668,087		Total H Admiss			Total Deaths	
		48,884		19,673		
Confirmed† 1,195,155	Probable† 472,932	Confirmed† 45,966	Probable† 2,918	Confirmed† 16,377	Probable† 3,296	

^{*} Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable).

here: https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/
Source: Cases - Virginia Electronic Disease Surveillance System (VEDSS) data entered by 5:00 PM the prior day

Outbreaks				
Total Outbreaks*	Outbreak Associated Cases			
7,252	123,394			

^{*} At least two (2) lab confirmed cases are required to classify an outbreak

Testing (PCR Only)					
Testing Encounters PCR Only*	Current 7-Day Positivity Rate PCR Only**				
13,134,925	3.2%				

^{*} PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."

^{**} Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data.

Multisystem Inflammatory Syndrome in Children				
Total Cases*	Total Deaths			
169	1			

^{*}Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 10:30am March 30, 2022 https://www.vdh.virginia.gov/coronavirus/

^{**} Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in Virginia.

[^]New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.

[†] VDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on August 27, 2020. Found

Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
 - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- Waning Immunity: Mean of 6 months to a year protection (rate of 0.0027) similar to Pfizer study, Omicron waning with a mean of 4 months
- Projection Scenarios:
 - Adaptive: Control remains as is currently experienced into the future with assumption that Omicron remains as the majority strain, and that infection with Omicron provides protection against Omicron infection in the future
 - Adaptive-VariantBA2: Same as Adaptive, but with BA.2 subvariant continuing predominance and having a 30% transmission advantage over existing Omicron
 - Adaptive-VariantBA2-IncreasedControl: Same as Adaptive-VariantBA2, but with a 25% reduction in transmission to increased mitigations starting on May 1st

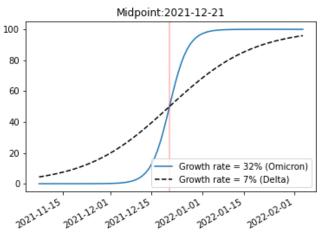


Scenarios – Omicron Description

Omicron shown ability to evade immunity and may be more transmissible

- Transmissibility: New evidence suggests that Omicron has similar transmissibility to Delta
- Immune Evasion: Strong evidence demonstrates that Omicron can cause infection in those with some immunity (natural and vaccine induced). Consensus estimate of 80% immune evasion allows Omicron to infect 80% of individuals that would have otherwise been protected against Delta. Assume that recovery from Omicron provides protection to infection with Omicron similar pre-Omicron variants
- **Prevalence**: Proportion of cases caused by Omicron variant estimated from growth rates observed in other countries with similar levels of immunity (growth of 32%, doubling in ~3 days)
- **Severity:** Several reports suggest Omicron may not cause as severe disease as Delta, we use a 50% reduction in severity for hospitalizations and deaths
- Studies: South Africa, UK, Canada

Estimated Prevalence curve for US



Predominance occurs before Jan 1, 2022

Scenarios – Omicron BA.2 Description

BA.2 shows signs of increased transmissibility

- **Transmissibility**: Analysis of household contacts in <u>Denmark</u> and the <u>UK</u> suggests a 40% to 3x increase in transmission.
- Now use a 30% boost to transmissibility only
- **Prevalence**: Detection in US has been widespread but limited; given growth observed elsewhere and US, and current estimated prevalence, this would lead to BA.2 prevalence of 50% in early April
- Severity: Assumed to be same as for other Omicron subvariants

Table 3: Relative effect of Omicron VOC BA.2 vs. BA.1

	Susceptibility			Transmissibility		
	Unvaccinated	Fully vaccinated	Booster vaccinated	Unvaccinated	Fully vaccinated	Booster vaccinated
Omicron BA.2 households	2.19	2.45	2.99	2.62	0.60	0.62
	(1.58-3.04)	(1.77-3.40)	(2.11-4.24)	(1.96-3.52)	(0.42 - 0.85)	(0.42 - 0.91)
Omicron BA.1 households	ref	ref	ref	ref	ref	ref
	(.)	(.)	(.)	(.)	(.)	(.)
Number of observations	17,945	17,945	17,945	17,945	17,945	17,945
Number of households	8,541	8,541	8,541	8,541	8,541	8,541

Notes: This table shows odds ratio estimates for the effect of living in a household infected with BA.2 relative to BA.1. Column 1 and 4 shows the relative transmission of BA.2, conditional on being unvac- cinated. Column 2 and 5 shows the relative transmission of BA.2, conditional on being fully vaccinated. Column 3 and 6 shows the relative transmission of BA.2, conditional on being booster vaccinated. Note, all estimates are from the same model, but with a different reference category across column 1-6. The estimates are adjusted for age and sex of the primary case, age and sex of the potential secondary case, size of the household, and primary case sample date. The estimates are furthermore adjusted for vacci- nation status of the potential secondary case and primary case interacted with the household subvariant. 95% confidence intervals are shown in parentheses. Standard errors are clustered on the household level. The odds ratio estimates for the full model are presented in Appendix Table 12, column 1

Danish Household Study - MedArxiv

Table 4. Secondary attack rates for contacts of cases with confirmed sequenced VUI-22JAN-01 and all other Omicron (VOC-21NOV-01)

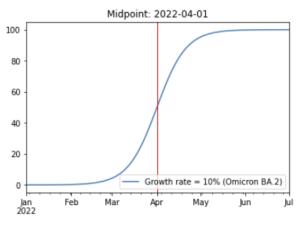
(Case test dates 1 January to 14 February 2022, variant data as of 7 March 2022 and contact tracing data as of 8 March 2022)

Variant	Setting	Number of exposing cases	Number of contacts	Adjusted* secondary attack rate (95% Confidence Interval)
VOC-21NOV-01	Household	178,069	369,011	10.7% (10.6%-10.8%)
VUI-22JAN-01	Household	20,072	41,621	13.6% (13.2%-14.0%)
VOC-21NOV-01	Non- household	30,325	74,343	4.2% (4.0%-4.3%)
VUI-22JAN-01	Non- household	3,565	8,763	5.3% (4.7%-5.8%)

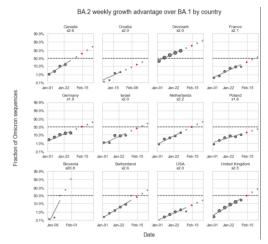
UK HAS report shows 2ndary Attack rates ~30% higher in households and out of households.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1060337/Technical-Briefing-38-11March2022.pdf

Estimated BA2 prevalence projection



This projected prevalence is based on the increase experienced in Denmark the growth rate in VA may be markedly different



Many countries Tracking a 2x Advantage for BA.2 vs. BA.1

Barak Raveh via Twitter

31-Mar-22 40

Projection Scenarios – Combined Conditions

Name	Txm Controls	Vax	Description
Adaptive	С	SQ	Likely trajectory based on conditions remaining similar to the current experience, includes immune escape due to Omicron
Adaptive-VariantBA2	С	SQ	Transmission rates for BA.2 infections are 30% more infectious, BA.2 prevalence reaches 50% on April 1 $^{\rm st}$ and rises to $^{\sim}95\%$ in next 4 weeks
Adaptive-VariantBA2- IncreasedControl	Increased	SQ	Same as Adaptive-VariantBA2 with increased mitigations reducing transmission by 25% starting May 1 st

Transmission Controls: C = Current levels persist into the future

Increased = Transmission rates are reduced by 25% over 2 weeks starting May 1st

Spring = Transmission rates from mid-Jan 2021 through mid-March 2021 are coarsely replayed,

representing a 60% reduction in transmission rate drivers, with Omicron remaining dominant

Vaccinations: SQ = Status quo acceptance leads to low rates of vaccination through the summer

VO = Vaccination acceptance optimistically expands with increased rates through the summer

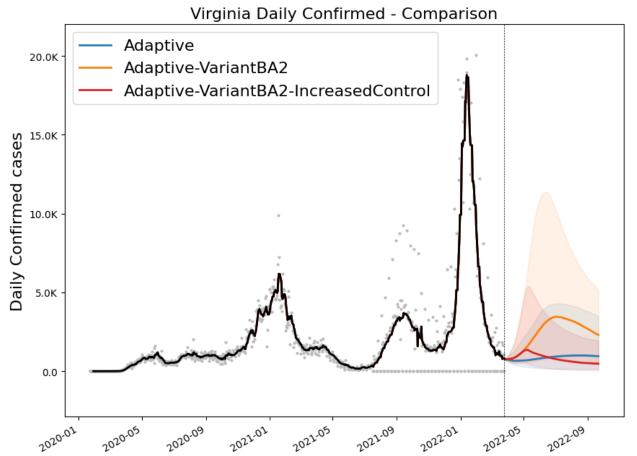
31-Mar-22 41

Model Results

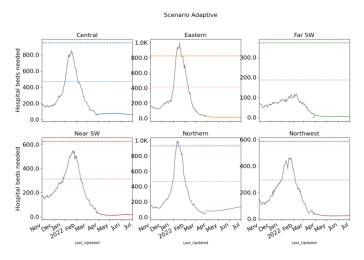


Outcome Projections

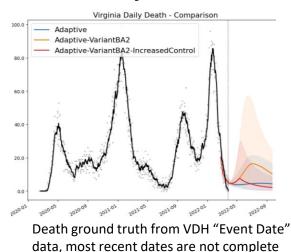
Confirmed cases



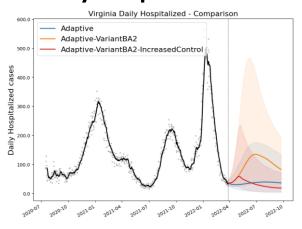
Estimated Hospital Occupancy



Daily Deaths



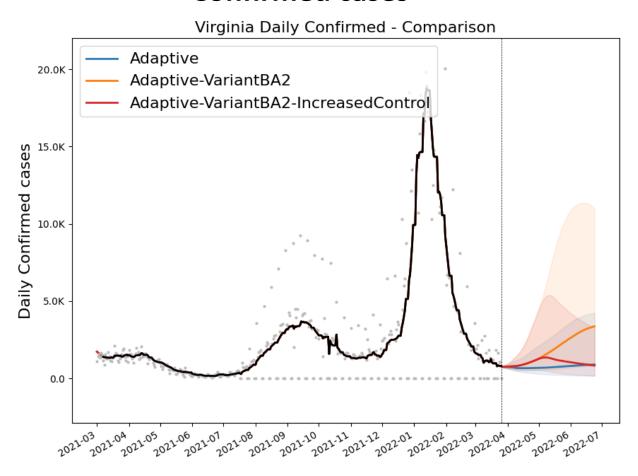
Daily Hospitalized





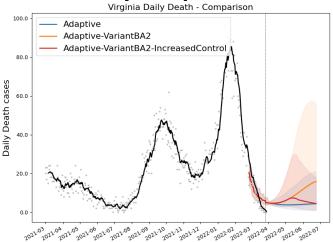
Outcome Projections – Closer Look

Confirmed cases

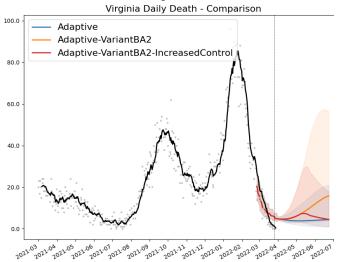




Daily Hospitalized



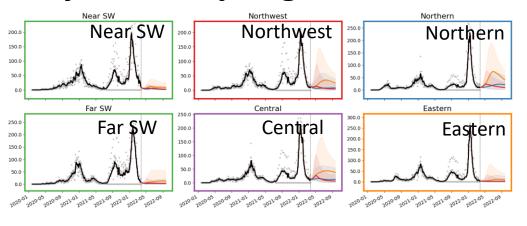
Daily Deaths



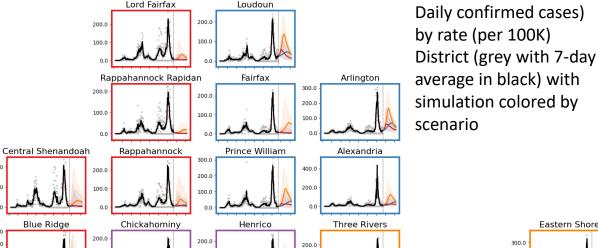
Death ground truth from VDH "Event Date" data, most recent dates are not complete

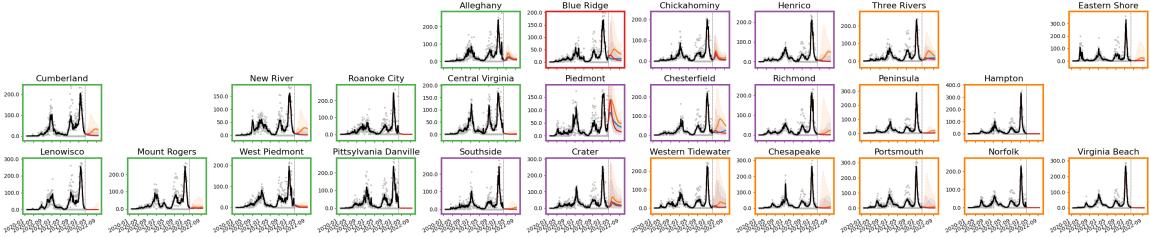
Detailed Projections: All Scenarios

Projections by Region



Projections by District

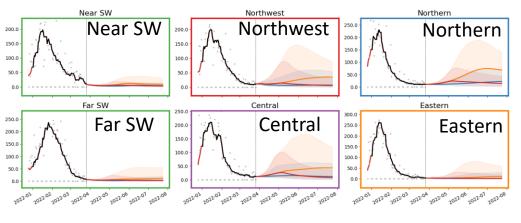




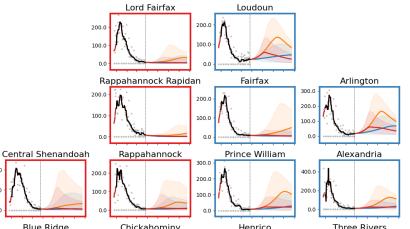


Detailed Projections: All Scenarios - Closer Look

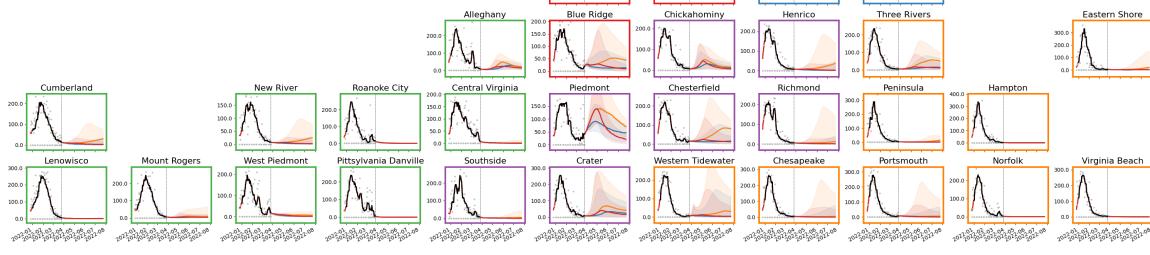
Projections by Region



Projections by District



Daily confirmed cases by rate (per 100K) District (grey with 7-day average in black) with simulation colored by scenario

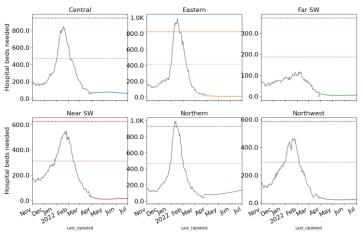


Hospital Demand and Bed Capacity by Region

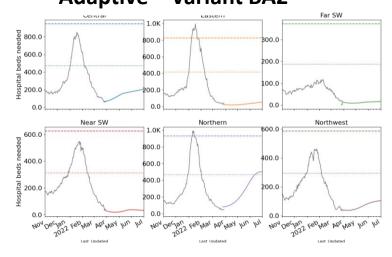
Capacities by Region

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds

Adaptive



Adaptive – Variant BA2



Length of Stay more variable with Omicron, occupancy projections may vary as a result, ad-hoc estimation performed per region

Estimated LOS stable

Projections show continued declines and with expanded capacities and adjusted length of stay, no capacities exceeded





Length of Stay Estimates

10

Central

Eastern

Far SW

Near SW

Northern

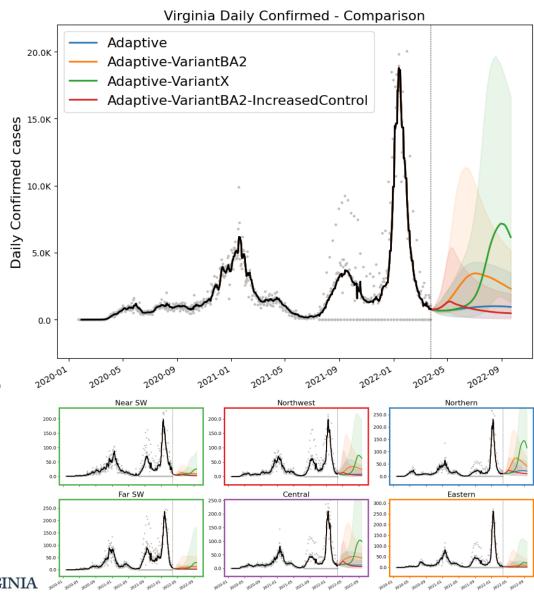
Northwestern

Unknown Future Variants

Currently there no known Variants expected to cause significant changes to current trajectories

- The risk remains, however, as Alpha, Delta, and Omicron have demonstrated.
- To explore what impact a speculative future variant might have we built a "Variant X" scenario, loosely based on the Alpha variant (eg Variant X is to Omicron as Alpha was to ancestral)
- Adaptive-VariantX: Same as Adaptive, with a 60% more transmissible variant arriving in mid-May and predominating (50% prevalence) by July 1

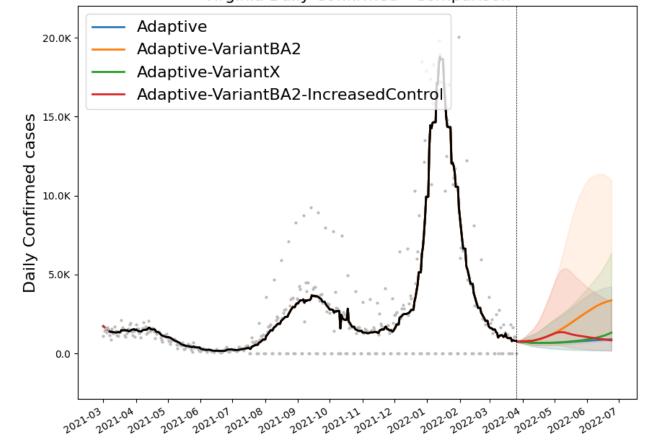
Confirmed cases



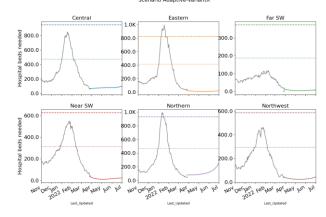
Unknown Future Variants – Closer Look

Confirmed cases

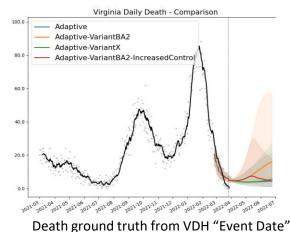




Estimated Hospital Occupancy

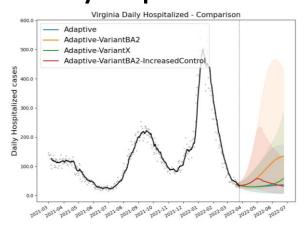


Daily Deaths



Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized

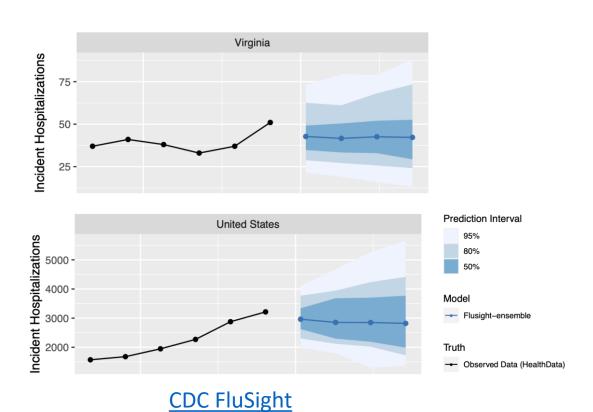




Current Influenza Hospitalization Forecast

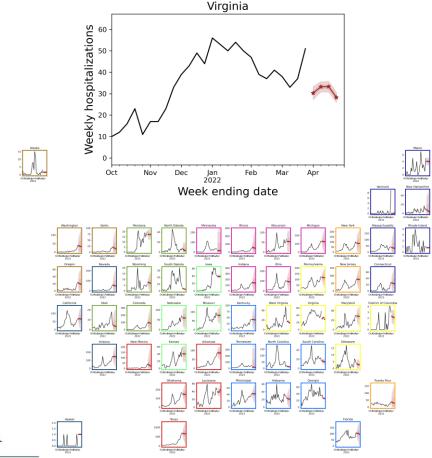
Statistical models for submitting to CDC FluSight forecasting challenge

Hospitalizations nationwide are rising, VA still steady



Ensemble Forecasts (Mar 14th)

Hospital Admissions for Influenza and Forecast for next 4 weeks (UVA ensemble)



Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rates and hospitalizations are starting to plateau
- VA 7-day mean daily case rate slowly decreased to 8/100K from 10/100K
 - US has plateaued to 9/100K (from 9/100K)
- BA.2 subvariant of Omicron approaches 50% prevalence and continues to grow
- Projections anticipate a plateau at moderate to low levels, though growth from BA.2 or other factors is possible:
 - Future levels and resilience to new variants and reduced infection control measures depend on the strength of immunity gained through infection with Omicron and its durability against waning
- Model updates:
 - Adjusted ascertainment levels during Omicron to better capture degraded case detection and reduced symptomatic fraction of Omicron
 - Further calibration of model parameters to match recent data on population immunity post-Omicron wave continue and will provide better longterm estimates of future disease dynamics

The situation continues to change. Models continue to be updated regularly.



Additional Analyses



Overview of relevant on-going studies

Other projects coordinated with CDC and VDH:

- Scenario Modeling Hub: Consortium of academic teams coordinated via MIDAS / CDC to that provides regular national projections based on timely scenarios
- Genomic Surveillance: Analyses of genomic sequencing data, VA surveillance data, and collaboration with VA DCLS to identify sample sizes needed to detect and track outbreaks driven by introduction of new variants etc.
- Mobility Data driven Mobile Vaccine Clinic Site Selection: Collaboration with VDH state and local, Stanford, and SafeGraph to leverage anonymized cell data to help identify

COVID-19 Scenario Modeling Hub

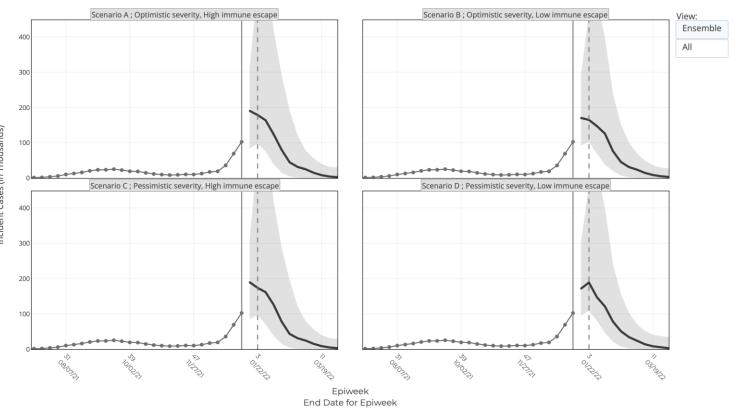
Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios that vary vaccine rates (high – low) and impact of the Delta variant (high and low)

- Round 12 recently released to assist in federal response to Omicron wave
- Only national consortium tracking
 Omicron wave well
- Rounds 4-11 now available

Round 4 Results were published May 5th, 2021 in MMWR

https://covid19scenariomodelinghub.org/viz.html

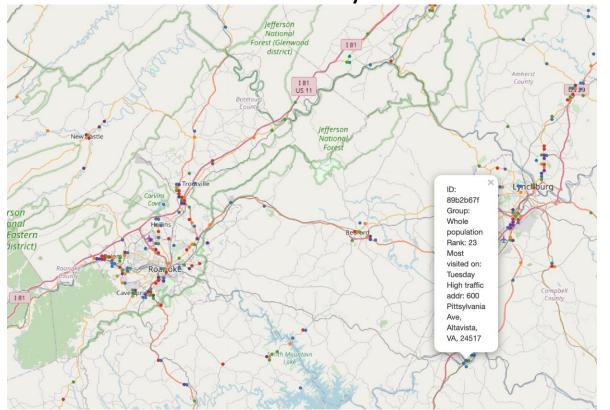
Projected Incident Cases by Epidemiological Week and by Scenario for Round 12 - Virginia (- Projection Epiweek; -- Current Week)



31-Mar-22

Data Recommended Mobile Vax Clinic Sites

Detailed and Timely Locations



Data Delivered and Disseminated to Locals

Provides a list of areas most visited by a given demographic group based on SafeGraph mobility data that links visits to specific sites and the home Census Block Group of the anonymized visitors

Demographic Groups: Black, Lantinx, Young Adults (20-40), Unvaccinated, and Whole Population

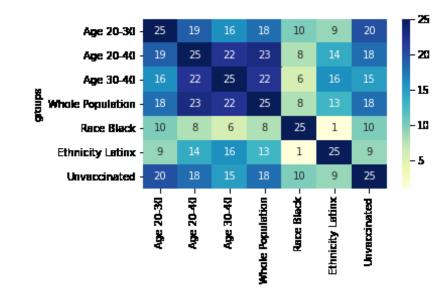
Data Included: Rank, Weight, most visited Day of Week, Highly Visited Address, and Lat-Long of area

Goal: Provide frequently visited locations based on populations and vaccination levels one desires to reach **Example:** List of location in the Southside frequented by 20-40 year olds



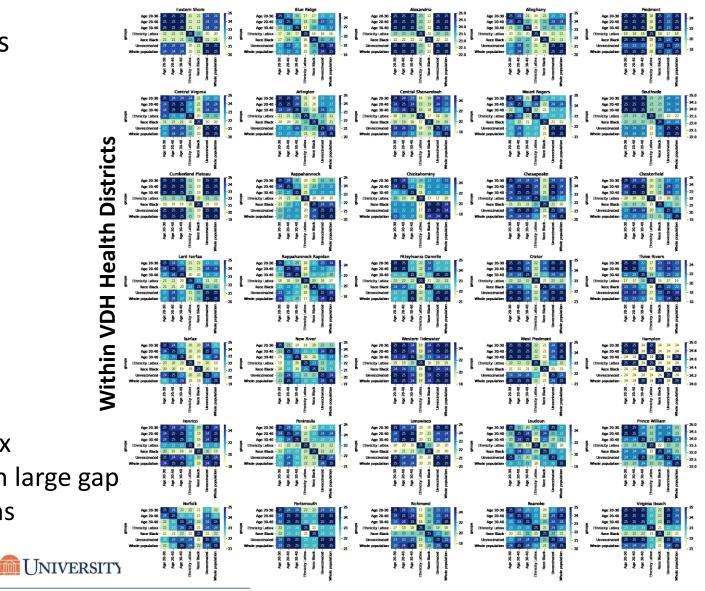
Data Recommended Mobile Vax Clinic Sites

Overlap of locations between groups



Different groups visit different areas

- Least overlap between Black and Latinx
- Overlap in ages highest, but drops with large gap
- Districts have different overlap patterns



State Level

References

Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

Arindam Fadikar, Dave Higdon, Jiangzhuo Chen, Bryan Lewis, Srinivasan Venkatramanan, and Madhav Marathe. Calibrating a stochastic, agent-based model using quantile-based emulation. SIAM/ASA Journal on Uncertainty Quantification, 6(4):1685–1706, 2018.

Adiga, Aniruddha, Srinivasan Venkatramanan, Akhil Peddireddy, et al. "Evaluating the impact of international airline suspensions on COVID-19 direct importation risk." *medRxiv* (2020)

NSSAC. PatchSim: Code for simulating the metapopulation SEIR model. https://github.com/NSSAC/PatchSim

Virginia Department of Health. COVID-19 in Virginia. http://www.vdh.virginia.gov/coronavirus/

Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/



Questions?

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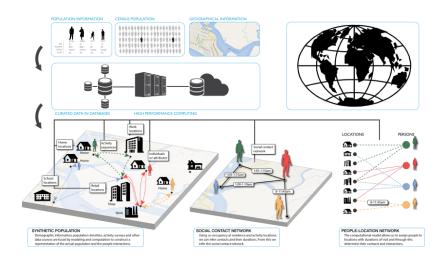
Supplemental Slides



Agent-based Model (ABM)

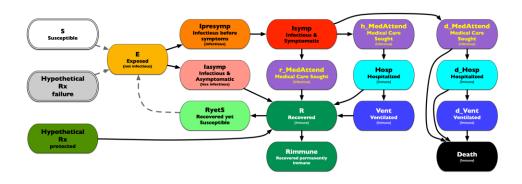
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments

